Medicine
TEAM 437

MED437
KING SAUD UNIVERSITY

Chronic Kidney Failure

Objectives :

- Differentiate Chronic kidney disease-CKD from Acute Kidney Injury-AKI.
- Describe the mechanism and pathophysiology of CKD progression and therapies to slow progression.
- Compare the different causes of CKD and the risk factors of progression.
- Identify recent updates in the diagnosis and therapy of CKD complications.
- Classify CKD into 5 stages.
- Discuss management choices of ESRD.

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Resources :

436 Team work

Doctor's notes

Master the Boards, Step-up to Medicine

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Function of normal kidneys:

MedEd video

- Fluid balance
- Electrolyte regulation
- Control acid base balance
- Waste removal Especially the nitrogenous products
- Hormonal function:

Acts as an endocrine organ and also a target for other hormones

  - ❏ Erythropoietin (the most important) get secreted from renal cell go to bone marrow ⟶ produce RBCs
  - ❏ Renin It plays a role in the blood pressure control (RAAS)
  - ❏ Prostaglandins
  - ❏ Active vitamin D3 vitamin D is synthesized in skin or we get it from food then it goes to the liver but its not in active form (25-hydroxycholecalciferol). After that, it goes to the kidney (target organ) to get activated into **1,25-dihydroxycholecalciferol**, which is the active form of Vit D.

Chronic kidney diseases:

CKD (CRF): chronic progressive **irreversible** (while AKI is reversible) loss of renal function. Its defined as the presence of clinical and/or pathologic evidence of kidney disease for **at least 3 months.**(less than that is considered as AKD)

ESRD: advanced CKD (stage-5) requiring dialysis or kidney transplantation

ESRD is defined as the loss of renal function leading to a collection of symptoms and laboratory abnormalities also known as uremia. Not defined as a particular BUN or creatinine.

Etiology of CKD: Extremely important. Memorize **in order,** especially the first three !

1. Diabetes mellitus 40% of cases (most common)
2. Hypertension 30% of cases.
3. Glomerulonephritis
4. Hereditary cystic and congenital renal disease (polycystic disease) 4% of cases
5. Interstitial nephritis / pyelonephritis 4% of cases
6. Miscellaneous 5% of cases
7. Tumors 2%

Risk factors for CKD:

1. Genetic (family hx of kidney disease) as polycystic kidney disease and Alport syndrome
2. Low socioeconomics status
3. Medical status(comorbidities) e.g.: diabetes, hypertension, obesity, CVD, **smoking.**

Stages of chronic kidney disease: depends on 1- presence evidence of kidney injury, 2- GFR

Stage	Description	GFR(ml/min/1.73m^2) normal:125
1	Kidney damage with normal or increased GFR You need evidence of kidney injury either by: 1-lab tests: high urea, high creatinine, hematuria, proteinuria or cast 2- radiological evidence like cyst, shrinking kidney, kidney scars, kidney stones or hydronephrosis, horseshoe kidney.	≥ 90 Normal person will have GFR more than 100 but we can **not** say he is in stage 1 until we have an **evidence of kidney injury**
2	Mild decrease in GFR + evidence of kidney injury	60-89
3	Moderate decrease in GFR+evidence of kidney injury divided into 3a: 45-59 . 3b: 30-44	30-59
4	Severe decrease in GFR + evidence of kidney injury	15-29
5	Kidney failure (ERSD)	<15 or dialysis

pathophysiology :

It occurs by two correlated mechanisms:

Compensation: increase of function and size

1- Loss of nephron mass ⟶ hypertrophy of the remaining nephrons

The hypertrophied nephron plasma flow and glomerular pressure increase (vasodilatation of the afferent Arterioles) if there is nephron loss there will be a reduction in GFR, the RAAS will be activated which will lead to dilation of the afferent arteriole and this will increase the intraglomerular pressure.

Enhance proximal reabsorption of NaCl, PO4 and fluids. Causing edema and hyperphosphatemia

Enhance collecting ducts secretion of K+ and H+

Normal GFR is 125ml/min, 70% is reabsorbed in proximal tubule, 20% in ascending loop, 5% in distal and 4% in collecting duct. Only 1 ml will pass in urine

These adaptation initially restore homeostasis.(by compensating Hyperkalemia and acidosis)

with hypertrophy the flow increases and so does the pressure. Prolonged high pressure on the basement membrane, would damage it. Leading to the loss of the nephron.

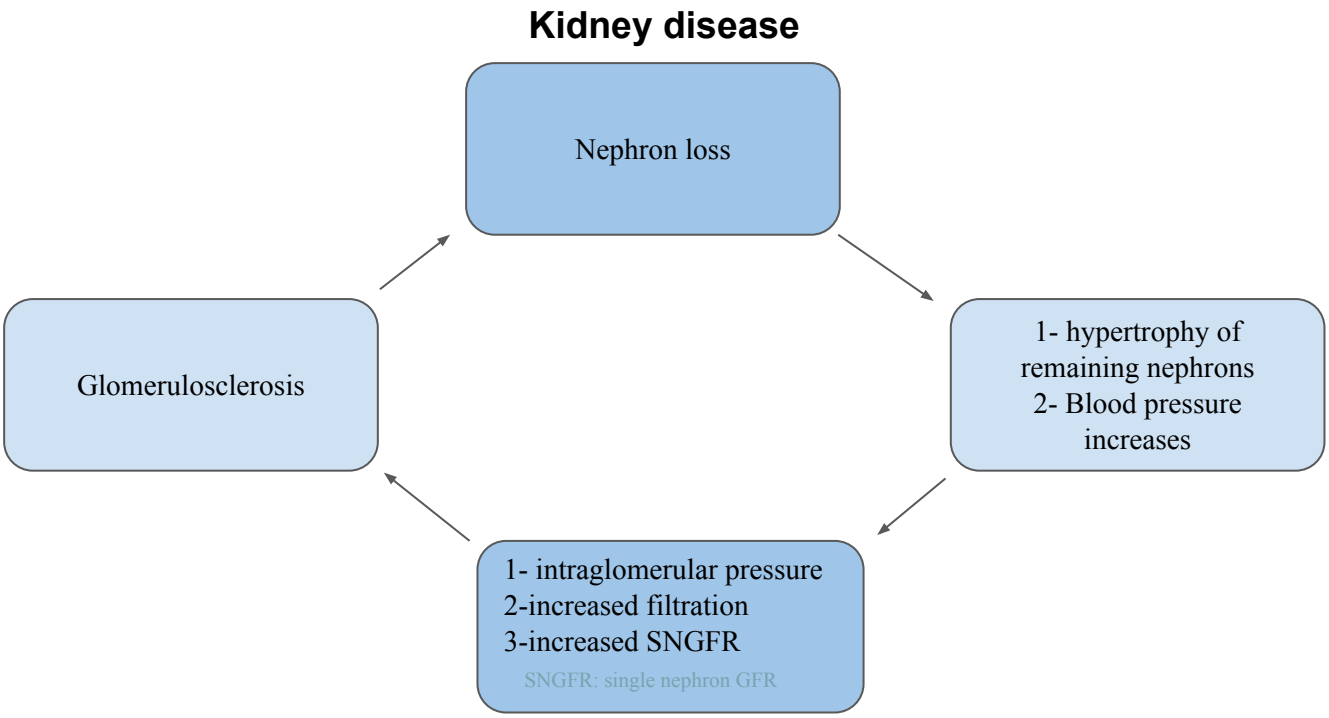
But glomerular hyperfiltration ⟶ glomerular injury ⟶ **glomerulosclerosis** ⟶ further loss of renal function

2- increase of some Growth factors such as: Increase in growth factors lead to tubulointerstitial disease, leading to interstitial fibrosis. Increased fibrosis means quicker progression to ESRD.

- Transforming growth factor B
- Platelets derived growth factors
- Osteopontin, angiotensin-II
- Endothelin

Ends with interstitial fibrosis

Vicious cycle of CKD that leads to ESRD:



Factors contributing to the progression of CKD:

We can not reverse the damage but we can delay the progression to other stage by controlling the factors

Important!

- **Hypertension**
- Proteinuria increase in urinary protein causes injury to tubular cells, leading interstitial inflammation and fibrosis. It depends on severity
- Hyperlipidemia
- Drugs (e.g. NSAID, aminoglycoside) if the pt is on any nephrotoxic drugs, stop it.
- High protein diet it leads to increase in intraglomerular pressure and hyperfiltration which lead to more damage
- Persistent metabolic acidosis
- Extent of tubulointerstitial disease. the more tissue involved, the worse outcome

Uremic syndrome:

Uremia results from retention of end products of protein metabolism. As urea and creatinine

- Administration of urea causes only mild symptoms.
- Other potential uremic toxins

-Guanidine
-P2 microglobulin
-Hippurate
-Homocysteine
-Parathyroid hormone (PTH)
-Phenols
-Phosphate
-Polyamines
-Purines
-Dimethyl arginine

Metabolic & electrolytes abnormalities in CKD:

1- carbohydrate intolerance:

- Insulin is degraded by the liver and kidneys
- The decrease in insulin clearance is offset by peripheral insulin resistance
- Hyperparathyroidism inhibits insulin secretion
- Decrease in requirements for insulin and oral hypoglycemic drugs in diabetic patients as they develop renal failure. Diabetic pts with ESRD come with the complaint of **hypoglycemic attacks** (dizziness, sweating and shivering). Direct indicator to decrease the dosage.

2- Dyslipidemia:

- Decrease in HDL cholesterol.
- Increase in TG (triglyceride) and lipoprotein A.

3- Fluid and electrolytes:

- Decrease GFR and defective tubular function causing expansion of plasma and ECF volumes, edema, and hypertension
- Hyponatremia can result from failure to excrete free water when intakes exceed 1.5L/day. Water intakes less than 0.5 L/day + increase salt intake leads to hypernatremia
- Hypertension is common unless Na+ intake is restricted to 100 meq/day. **HTN is caused commonly by the fluid and Na retention.**
- Patients with salt losing nephropathy require stepwise increases in NaCl and fluid intake.
- K+ elimination in CKD is initially maintained by: limited role
  a- enhanced K+ secretion in surviving nephrons hypertrophy
  b- colonic K+ secretion (from aldosterone stimulated by hyperkalemia and metabolic acidosis).in the beginning of kidney failure the colon will start to secret K+. normally it will not secret K+ because the kidney usually does this job. Colon can only secrete 20% of the total body K load, overtime it'll shut off, leading to hyperkalemia.
  However, as GFR decreases, K+ elimination is curtailed which lead to hyperkalemia

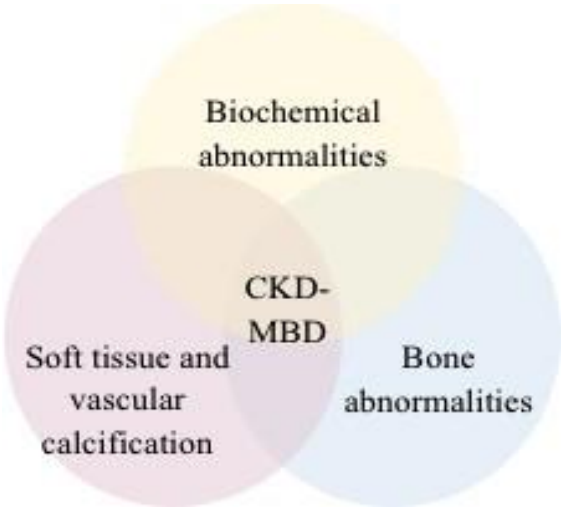
4- Acid-base abnormalities (metabolic acidosis)

- The body produces about 80 mmol of non-volatile from metabolism everyday.
- These acids accumulate as renal failure progresses
- Production of ammonia NH3 (im distal and CD cells) decreases which limits distal tubular H+ trapping as NH4 and hence, decreased renal bicarbonate regeneration (H is secreted from the body when it combine with NH3 becoming NH4, if we have a kidney injury no NH3 production this will lead to accumulation of H+(acidosis))
- Additionally , there may be proximal HCO3 wasting or reduced distal H+ secretion. Less important factor. **The first three are the most important**

Chronic kidney disease-mineral and bone disorder (CKD-MBD):

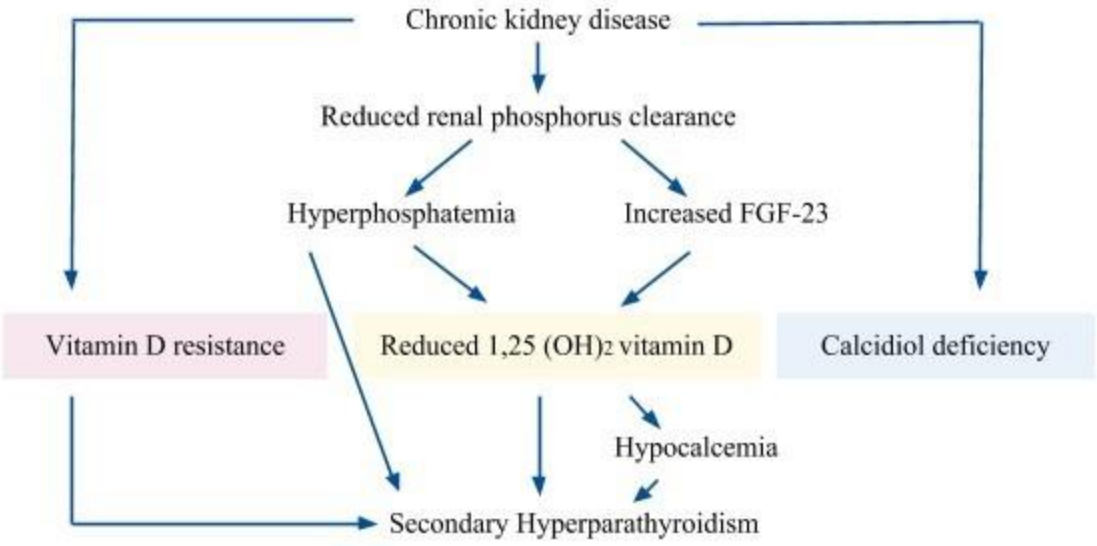
Indicates alteration in mineral bone metabolism. These alteration include:

- Biochemical abnormalities in calcium, phosphorus, PTH, vitamin D and fibroblast growth factor-23.
- Changes in bone morphology: volume, turnover, and mineralization.
- Calcification of soft tissue and blood vessels important because it causes increase in mortality (ie heart attacks)



CKD-MBD Pathogenesis:

- As GFR declines, the excretion of phosphorus is impaired, leading to phosphate retention.
  The phosphorus excretion is **only** through the kidney.
  - ❑ Hyperphosphatemia is an independent risk factor for the increased morbidity and mortality of stage 5 CKD from cardiovascular events
- Recently, it has been demonstrated that fibroblast growth factor 23(FGF-23)which is secreted by osteocytes is stimulated by phosphorus retention
  - ❑ FGF-23 causes phosphaturia (stimulate kidney to excrete PO2) and maintains serum phosphorus in the normal range until GFR declines to < 30 ml/min/1.73m2
  - ❑ FGF-23 also decreases 1.25-dihydroxy vitamin D (calcitriol) formation which in conjunction with hyperphosphatemia, will lead to parathyroid hyperplasia and an increase in PTH secretion



So hyperphosphatemia lead to direct effect to **secondary hyperparathyroidism**(increase secretion of PTH) and indirect effect by decrease 1,25-dihydroxyvitamin D which lead to hypocalcemia leads to strong stimulator to parathyroid gland leads to hyperparathyroidism

The classic biomedical abnormalities: what we see in blood analysis

- Hypocalcemia
- Hyperphosphatemia
- Hyperparathyroidism
- Hypovitaminosis D
- Elevated FGF-23

Bone abnormalities = renal osteodystrophy (ROD):

It's a complex disorder of bones in uremic patient resulting from abnormalities of mineral ions (Ca, Po4, Mg), PTH, Vit D, and FGF23 metabolism in the presence of factors related to the uremic state.

- Spectrum of bone abnormalities in ROD:
  1-Osteitis fibrosa cystica (high bone turnover)
  Due to: a-increased activity of both osteoclast and osteoblast
  b- increased PTH
  2-Adynamic bone disease (low bone turnover)
  3-osteomalasia (low turnover accompanied by under mineralized bone tissue)
  4-combination of the above
- Patients with these bone abnormalities may be asymptomatic or may develop symptoms related to **bone pain** or **fractures**
- ESRD patients on dialysis have > 3-4 times increased risk of vertebral and hip fractures compared to general population even after adjustment for age, gender and race.

Low calcium leads to secondary hyperparathyroidism. High parathyroid hormone levels remove calcium from bones, making them soft and weak.

Adynamic bone disease:

Risk factors:

- Advanced age
- CAPD (continuous ambulatory peritoneal dialysis)
- Diabetes mellitus
- Calcitriol therapy
- Parathyroidectomy
- Fluoride and iron intoxication

Mechanism:

Defect in osteoblast development or activity caused by factors related to the uremic state

Cardiovascular abnormalities of ESRD (CKD-5)

CKD pts won't die from kidney failure, but due to CVS abnormalities

Hypertension (most common) The immune system (lymphocytes) helps keep arteries clear of lipid accumulation. White blood cells don't work normally in a uremic environment. Leading to accelerated atherosclerosis and hypertension. This is the most common cause of death in those on dialysis.	1-occurs in 90% of patients with ESRD 2-Secondary to salt and water retention **(the primary cause)** 3-inappropriate activation of RAAS 4-increased sympathetic tone 5-increase generation of vasoconstriction (endothelin) 6- decrease generation of vasodilators (nitric oxide)	1- These abnormalities increase 2-5 folds in ESRD. 2- About one-half of all hemodialysis patients have significant ischemic heart disease. 3- Dyslipidemia, HTN, increased homocysteine, DM, and insulin resistance contribute to atherosclerosis 4- Anemia aggravate LVH 5- Hyperparathyroidism, amyloidosis, and iron overload cause also cardiac dysfunction.
cardiomyopathy	1-Left ventricular hypertrophy (LVH) 2-coronary artery Disease (CAD) Angina + MI due to vascular and soft tissues calcification, especially in coronary arteries, carotid and cerebral arteries. 3-Congestive heart failure (CHF) ⟶ Diastolic Dysfunction	
Pericarditis and pericardial effusion	Due to uremia pericardial effusion (blood) یکون مدمی this is an indication for dialysis	skipped by the doctor

Neuromuscular abnormalities:

1-CNS dysfunction

- Decreased attention, agitation, confusion, insomnia, and impaired memory
- May develop also: depression, hallucination, delusion, **hiccups**, cramps, flapping tremor usually it's one of three things liver failure, renal failure, and respiratory failure(CO2 retention), myoclonus, fasciculation, and seizures. (Seizure and coma usually present in advanced cases)
- Flapping tremor and hiccups are important sign for **encephalopathy** ⟶ Emergency dialysis

2-Peripheral neuropathy

- Usually symmetric, lower limbs. Bilateral
- Sensory precedes motor dysfunction.
- Restless leg syndrome and burning feet — neuropathic pain in the legs that is only relieved with movement.
- Postural hypotension (autonomic dysfunction)

Hematologic abnormalities:

1-Anemia

- Develops as serum creatinine increases > 180 mcm/L and GFR declines to < 30 ml/minute
- Normocytic, normochromic anemia before they start dialysis but once they start it, they will develop Iron Deficiency Anemia because they may lose blood during the procedure
- Main cause: decrease production of EPO

2-Platelet dysfunction

- Bruising, ecchymoses, bleeding from mucous membrane
- Platelet dysfunction (count is **normal**): low VWF (VWF lies in the storage granules, the platelets do not release their granules in uremic environment so there will be a decrease of VWF in the blood) which facilitate the interaction between platelets and endothelium through its binding to platelet glycoprotein (IIb,IIIa) receptors. You evaluate the platelet function by **bleeding time** (up to 10 mins is normal) if more, you have to be careful with biopsy or any surgical procedure. Other tests will be NORMAL
- Platelets don't work normally in a uremic environment. They do not degranulate. If a platelet does not release the contents of its granules, it will not work.

Gastrointestinal abnormalities: VERY COMMON

- Anorexia, nausea, and vomiting
- Uremic fetor (urine smell in their mouth) , stomatitis, esophagitis, and peptic ulcer disease, Gastritis
- Increased gastrin in CKD (it is the **cause** of stomatitis, esophagitis, and peptic ulcer disease)

Dermatological abnormalities:

Uremic pruritus is related to:

- Calcium and phosphate deposition (secondary to increased PTH)
- Hypercalcemia.
- Peripheral neuropathy
- Dry skin. That's why pts ar adviced to moisturize their skin
- Anemia
- Inadequate dialysis

Natural Hx of CKD:

Early: usually asymptomatic in its early stages.
Late: symptoms and signs usually related to:

- Sodium and water retention ⟶ HTN, edema.
- Metabolic and hormonal complication ⟶ Anemia, Vit D deficiency, increase PTH.
- Increased incidence of CVD, infection, and impaired physical function

Evaluation of patients with CKD:

doctor didn't focus on it

- The history should document the presence of uremic symptoms and possible etiology from: Diabetes Mellitus, Hypertension, Congestive heart failure, MM, NSAID.
- Family history can suggest PCKD (polycystic kidney disease) or hereditary nephritis.
- Volume depletion and obstructive nephropathy should be identified and treated promptly.
- **Ultrasound: small, shrunken kidneys.**
- **Normal kidney size with CKD: DM, amyloid, MM.**

All patients with CKD should have a basic evaluation including:

Test	Indication
Serum creatinine	The first appropriate test to do when you suspect CKD
CBC	Normocytic, normochromic anemia
Urinalysis	1-Proteinuria risk of progressive CKD requiring preventive ACE inhibitor or ARB therapy 2-Hematuria ⟶ ⟶
Urea and electrolytes	Uremia, hyperkalemia, hypocalcemia, hypermagnesemia, and hyperphosphatemia
PTH	Secondary hyperparathyroidism
Vit-D	Hypovitaminosis D
Cr clearances	To estimate GFR
Renal ultrasound	To evaluate size of kidneys/rule out obstruction
Urine pro/cr ratio	
LFTs	

Further evaluation will depend on initial findings and likely diagnostic possibilities

Management of patients with CKD:

1- Nutrition:	Restriction intake of: • Protein, not less than 0.8 - 1 mg/kg/day to avoid malnutrition. Pts on dialysis will increase their intake (1.2 - 1.3 mg/day) • Phosphate • Sodium (to avoid hypertension) • potassium
2- Salt and water retention:	• Salt intake restriction - daily Na+ <100 meq. NaCl intake would be 2-2.4 g/day • Fluid restriction 1 - 1.5 L/day • Loop diuretics • RAAS inhibition (ACE, ARB) if HTN w/proteinuria
3- Hyperkalemia:	• Exogenous sources of K+: dates, dried fruits, citrus fruits, banana, chocolate, and salt substitute (ie potassium chloride) . It is the first you check! • Medication that increase K+: ACEI,ARB,NSAID, K+ - sparing diuretics, B-BLOCKERS, and Heparin Treatment of hyperkalemia: 1. IV calcium gluconate 10 cc of 10% (first step, it works by shifting K+ into the cells) protection of cardiac cells 2. Followed by 25 ml of 50% dextrose solution with 5-10 units regular insulin 3. B2-adrenergic agonist nebulizer (salbutamol). It used as second step if the first fails 4. NaHCO3 IV/oral If all fails and hyperkalemia is refractory then we should consider dialysis.
4- Hyperphosphatemia and secondary hyperparathyroidism	**A**-Reduce phosphate intake to < 10 mg/kg/day. **B**-Phosphate Binders: calcium carbonate(given to Pt with low Ca), Sevelamer (Renagel), Lanthanum carbonate (given to patient with highl normal Ca). our food full of PO4 so we give them this drug it will bind to phosphate and excreted in feces. **C**-Vitamin D (calcitriol) 0.125 mcq/day • Must be withheld until s. Phosphate concentration have been controlled to < 6 mg/dl because it may cause severe soft tissue calcification. • Vitamin D compounds can cause hypercalcemia and hyperphosphatemia, which may increase coronary calcification, so: paricalcitol (zemplar) is analogue (calcimimetic) that inhibits PTH synthesis without elevation of calcium/phosphates. **D**-Indication for parathyroidectomy: PTH > 800 pg/ml with symptoms of bone disease (myopath, bonepain) persistent hyperphosphatemia soft tissue calcification.
5- Hyperlipidemia	The goal is to keep low density lipoprotein cholesterol < 100 mg/dl by diet control and statin group

6- Anemia	1-Target Hb/Hct: - K DOQI ⟶ Hemoglobin 11-12 hematocrit 33-36%. ● Anemia will cause left ventricular hypertrophy, decrease quality of life and reduces survival of patients on HD. ● Conversely: Hb > 13 and Hct > 42 are associated with more coronary events and increased mortality as evidenced by CHOIR (USA) and CREATE (Europe) studies. That's why our Hb goal isn't the normal range 2-Target iron levels: Based on ferritin and T-SAT levels in the blood, we decide to give or not to give Iron supplements ● Percent transferrin saturation (T-SAT) reflects iron available for erythropoiesis. ● Serum ferritin reflects over all iron stores. ● In CKD, target T-Sat > 20 (20-50). ● Target S.ferritin > 100 ng/ml ● Iron supplement should be withheld, if T-sat > 50, S.ferritin > 800 ng/ml

Treatment Guidelines (Anemia) important!

1- Oral iron

- In non-dialysis patients (CKD stages 1-4):

100-200 mg elemental iron should be given daily after meals. (1 tab Ferrous Fumarate, 200 mg contains 66 mg elemental iron)

2- IV iron:

1 gr of iron saccharate (ferosac) divided into 10 doses of 100 mg given with each dialysis session.

- In dialysis patients (CKD 5):

IV iron should be given as ongoing iron losses tends to be higher

3-Recombinant Erythropoietin-epoetin alfa (eprex) (short acting):

- Patients on starting dose 120-180 IU/kg/week, IV
- Pre-dialysis patients and PD patients: 120-80 IU/kg/week subcutaneously weekly dose - Hb/Hct monitoring every 4 weeks. The aim is to keep Hb around 11-12

The most common side effects are: headache, HTN, arthralgia, AND diarrhea.

4-Recombinant Erythropoietin-Darbepoetin Alfa (Aranesp) good for pts of peritoneal dialysis. Also, for those who are not on dialysis (still stage IV)

- Half-life: three fold longer IV and two fold longer S/C than of epoetin
- Recommended starting dose 0.45 mcg/kg S/C weekly or double the dose every 2 weeks
- Pre-filled injections: 20,40,60,80 mcg stored in the fridge

Resistance to epoetin:

1- Inadequate Epo dose

2- Anemia of chronic disease (infection, inflammation)

3-Functional iron deficiency

4- Secondary to hyperparathyroidism

5- Carnitine deficiency

6-Hemoglobinopathies

7- Aluminum toxicity

8- B12/ folate deficiency

9- Malnutrition

Managements of ESRD:

1- conservative management. (Ie fluids, salt, potassium, phosphorus, etc..)

2-Hemodialysis-HD

- Vascular access: AVF, AVG, Permcath

3- Peritoneal Dialysis - PD skipped

- CAPD, CCPD, NIPD

4- Kidney Transplantation only cure

- Living related, Living unrelated, Cadaveric

Summary

Chronic Kidney Disease	
Etiology	Diabetes mellitus in 40% of cases. Hypertension in 30% of cases. Glomerulonephritis in 15% of cases and other causes.
Stages	1. Kidney damage with normal or ↑ GFR (≥ 90) 2.Mild ↓GFR (60-89) 2. Moderate ↓ GFR (30-59) 3. Severe ↓ GFR (15-29) 4. Kidney failure, (ESRD) GFR: <15 or dialysis
Mechanism and pathophysiology	1. Loss of nephron mass → hypertrophy of the remaining nephrons the hypertrophied nephron plasma flow and glomerular pressure increase (vasodilatation of the afferent Arterioles) > ↑ Intraglomerular pressure (due to ↑ blood supply) and ↑ Filtration (still the total GFR is decreased). ➔ Enhance proximal reabsorption of NaCl, Fluids and PO4. causing edema and hyperphosphatemia ➔ Enhance collecting ducts secretion of K+ and H+ These adaptations initially restore homeostasis. 2. Increase of some Growth factors such as: Transforming growth factor-B, Platelets derived growth factors, Osteopontin, angiotensin-II, Endothelin. leading to further kidney damage and interstitial fibrosis.
Factors contributing progression	Degree of hypertension, Severity of proteinuria, Hyperlipidemia, Drugs (NSAIDs, aminoglycoside), High protein diet, Persistent metabolic acidosis, Extent of tubulointerstitial disease.
Changes in other body systems	1. CVS changes: HTN, Cardiomyopathies, pericarditis due to uremia and CHF 2. Neuromuscular: CNS dysfunction (Decreased attention and agitation...) And peripheral neuropathy 3. Hematologic: Anemia that develops as serum creatinine increases And platelet dysfunction with normal count and low VWF 4. GI: Anorexia, nausea and vomiting 5. . Dermatologic: Uremic pruritus
Management	Management: Restriction of protein, phosphate, sodium and potassium intake. Salt and water restriction RAAS inhibition if required. Reduce phosphate intake to < 10 mg/kg/day, Vitamin D (Calcitriol) 0.125 mcq/day, The goal is to keep low density lipoprotein cholesterol < 100 mg/dl by diet control and statin group, Control anemia.

- CKD (CRF) means: chronic progressive irreversible loss of renal function. It is defined as the presence of clinical and/or pathologic evidence of kidney disease for at least 3 months.
- ESRD: advanced CKD (Stage-5 (last stage)) requiring dialysis or kidney transplantation, happens secondary to water and salt retention which is one of the leading causes of developing it.
- Fluid and electrolytes of the body get disrupted during CKD there will be: Decreased GFR leading to plasma and ECF expansion, Hyponatremia and Hypertension (unless sodium intake is restricted to 100 meq/day)

Questions

1. **A 50-year-old man comes to the physician for a routine follow-up visit. He has hypertension, diabetes mellitus, secondary hyperparathyroidism, and end-stage renal disease. He has been on hemodialysis for the past three years. He was admitted three months ago for line sepsis, which was treated with antibiotics. He had a right below-the-knee amputation two years ago following a non-healing foot ulcer. Physical examination shows a right carotid bruit. If this patient dies within the next five years, what would be the most likely cause of his death?**
   A. Cardiovascular disease
   B. Stroke
   C. Infection
   D. Cancer

2. **Which substances of the following do the kidney produces?**
   A. 25 - hydroxycholecalciferol , prostaglandins PGE2 , Erythropoietin
   B. 25 - hydroxycholecalciferol , prostaglandins PGE2 , aldosterone
   C. Angiotensin converting enzyme , Erythropoietin , prostaglandins PGE2
   D. Angiotensin converting enzyme , aldosterone , prostaglandins PGE2

3. **Typical Biochemical features of chronic kidney failure includes?**
   A. Hypophosphatemia
   B. Hypercalcemia
   C. Metabolic acidosis
   D.Polyuria

4. **At a routine checkup, a 42-year-old male with diabetes is found to have an eGFR of 32 ml/min/1.73 m2. When repeated 3 months later, it is 35 ml/ min/1.73 m2. His albumin:creatinine ratio (ACR) is 35 mg/mmol (310 mg/g). Macroalbuminuria is defined as ACR >30 mg/mmol (>300 mg/g). What stage of CKD does he have?**
   A. Stage 1
   B. Stage 2
   C. Stage 3
   D.Stage 4

5. **Which of the following statements about parathyroid hormone synthesis is true?**
   A. It is stimulated by activated vitamin D3
   B. It is stimulated by hypocalcaemia
   C. It is inhibited by hyperphosphatemia
   D.It is inhibited by FGF-23

6. **All of the following describe the natural history of Chronic kidney disease Except?**

A. hyperfiltration of non-injured nephrons cause eventual sclerosis
B. Hypertension develops as consequence of CKD
C. Proteinuria itself contribute to glomerular damage and progression of chronic kidney disease
D. progression of chronic kidney disease is reversible depending on the underlying cause

7. **A 49-year-old woman attends your clinic suffering from chronic renal failure due to progressive glomerular disease. She appears well and her blood pressure is 141/92 mmHg. Blood tests reveal elevated phosphate, serum creatinine and urea, while calcium levels are low. Her estimated glomerular filtration rate is 35 mL/min/1.73m2. You also notice the patients cholesterol levels are moderately raised. The most appropriate management is:**

A. Sevelamer
B. Parathyroidectomy
C. Oral vitamin D
D. Cinacalcet

Answers:
1.A
2.C
3.C
4.C
5.B
6.D
7.A